IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	
NI *et al.*	Art Unit: *To be assigned*
Appl. No. *To be assigned* (Divisional of Appl. No. 09/042,583; Filed: March 17, 1998)	Examiner: *To be assigned*
Filed: *Herewith*	Atty. Docket: 1488.131000A/EKS/EJH
For: **Death Domain Containing Receptor 5**	

Preliminary Amendment

Commissioner for Patents
Washington, D.C. 20231

Box: Patent Application

Sir:

In advance of prosecution, Applicants respectfully request that the application be amended. This Amendment is provided in the following format:

(A) A clean version of each replacement paragraph/section/claim along with clear instructions for entry;

(B) Starting on a separate page, appropriate remarks and arguments. 37 C.F.R. § 1.115; and

(C) Starting on a separate page, a marked-up version entitled: "Version with markings to show changes made."

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments

Inventorship:

Please delete Jeffrey Su as an inventor.

In the Specification:

Please insert the following priority information below the heading "Field of the Invention" on page 1:

This present application is a divisional of U.S. Appl. No. 09/042,583, filed March 17, 1998, which claims the benefit of U.S. Provisional Appl. Nos. 60/040,846, filed March 17, 1997, and 60/054,021, filed July 29, 1997. All of said applications are herein incorporated by reference.

Please delete the entire paragraph at page 1, lines 12-14.

Please replace the paragraph beginning at page 6, line 30 with the following paragraph:

FIG. 4 shows the nucleotide sequences (HAPBU13R (SEQ ID NO:6) and HSBBU76R (SEQ ID NO:7)) of two cDNA molecules which are related to the nucleotide sequence shown in Figure 1 (SEQ ID NO:1).

Please replace the paragraph beginning at page 7, line 20, with the following paragraph:

The present invention provides isolated nucleic acid molecules comprising a polynucleotide encoding a DR5 polypeptide having the amino acid sequence shown in FIG. 1 (SEQ ID NO:2), or

a fragment of the polypeptide. The DR5 polypeptide of the present invention shares sequence homology with other known death domain containing receptors of the TNFR family including human TNFR- I, DR3 and Fas (FIG. 2). The nucleotide sequence shown in FIG. 1 (SEQ ID NO:l) was obtained by sequencing cDNA clones such as HLYBX88, which was deposited on March 7, 1997 at the American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209, and given Accession Number 97920. The deposited clone is contained in the pSport 1 plasmid (Life Technologies, Gaithersburg, MD).

Please replace the paragraph beginning at page 9, line 25, with the following paragraph:

In the present case, the predicted amino acid sequence of the complete DR5 polypeptide of the present invention was analyzed by a computer program ("PSORT"). S*ee,* K. Nakai and M. Kanehisa, *Genomics 14*:897-911 (1992). PSORT is an expert system for predicting the cellular location of a protein based on the amino acid sequence. As part of this computational prediction of localization, the methods of McGeoch and von Heinje are incorporated. The analysis by the PSORT program predicted the cleavage sites between amino acids 51 and 52 in Figure 1 (-1 and 1 in SEQ ID NO:2). Thereafter, the complete amino acid sequences were further analyzed by visual inspection, applying a simple form of the (-1,-3) rule of von Heinje. von Heinje, *supra.* Thus, the leader sequence for the DR5 protein is predicted to consist of amino acid residues from about 1 to about 51, underlined in Figure 1 (corresponding to about -51 to about -1 in SEQ ID NO:2), while the predicted mature DR5 protein consists of residues from about 52 to about 411 in Figure 1 (corresponding to about 1 to about 360 in SEQ ID NO:2).

Please substitute the paragraph beginning at page 12, line 19, with the following paragraph:

In another aspect, the invention provides an isolated nucleic acid molecule comprising a polynucleotide which hybridizes under stringent hybridization conditions to a portion of the polynucleotide in a nucleic acid molecule of the invention described above, for instance, the cDNA clones contained in ATCC Deposit No. 97920. By "stringent hybridization conditions" is intended overnight incubation at 42°C in a solution comprising: 50% formamide, 5x SSC (750 mM NaCl, 75 mM tri sodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 μg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1x SSC at about 65°C.

In the Claims:

Please cancel claims 1-34 without prejudice or disclaimer.

Please add the following new claims 35-179:

35. (New) An isolated polypeptide comprising an amino acid sequence at least 90% identical to amino acids 1 to 360 of SEQ ID NO:2, wherein said polypeptide binds TNF-related apoptosis-inducing ligand (TRAIL).

36. (New) The polypeptide of claim 35, which induces apoptosis.

37. (New) The polypeptide of claim 35, comprising an amino acid sequence at least 95% identical to amino acids 1 to 360 of SEQ ID NO:2.

38. (New) The polypeptide of claim 35, which is produced by a recombinant host cell.

39. (New) The polypeptide of claim 38, wherein said recombinant host cell is a eukaryotic host cell.

40. (New) The polypeptide of claim 35, which comprises a heterologous polypeptide.

41. (New) The polypeptide of claim 40, wherein said heterologous polypeptide comprises an immunoglobin Fc region.

42. (New) The polypeptide of claim 41, wherein said immunoglobin Fc region is a human immunoglobin Fc region.

43. (New) A composition comprising the polypeptide of claim 35, and a carrier.

44. (New) An isolated polypeptide comprising an amino acid sequence at least 90% identical to amino acids -50 to 360 of SEQ ID NO:2, wherein said polypeptide binds TNF-related apoptosis-inducing ligand (TRAIL).

45. (New) The polypeptide of claim 44, which induces apoptosis.

46. (New) The isolated polypeptide of claim 44, comprising an amino acid sequence at least 95% identical to amino acids -50 to 360 of SEQ ID NO:2.

47. (New) The polypeptide of claim 44, which is produced by a recombinant host cell.

48. (New) The polypeptide of claim 47, wherein said recombinant host cell is a eukaryotic host cell.

49. (New) The polypeptide of claim 44, which comprises a heterologous polypeptide.

50. (New) The polypeptide of claim 49, wherein said heterologous polypeptide comprises an immunoglobin Fc region.

51. (New) The polypeptide of claim 50, wherein said immunoglobin Fc region is a human immunoglobin Fc region.

52. (New) A composition comprising the polypeptide of claim 44, and a carrier.

53. (New) An isolated polypeptide comprising an amino acid sequence at least 90% identical to amino acids -51 to 360 of SEQ ID NO:2, wherein said polypeptide binds TNF-related apoptosis-inducing ligand (TRAIL).

54. (New) The polypeptide of claim 53, which induces apoptosis.

55. (New) The polypeptide of claim 53, comprising an amino acid sequence at least 95% identical to amino acids -51 to 360 of SEQ ID NO:2.

56. (New) The polypeptide of claim 53, which is produced by a recombinant host cell.

57. (New) The polypeptide of claim 56, wherein said recombinant host cell is a eukaryotic host cell.

58. (New) The polypeptide of claim 53, which comprises a heterologous polypeptide.

59. (New) The polypeptide of claim 58, wherein said heterologous polypeptide comprises an immunoglobin Fc region.

60. (New) The polypeptide of claim 59, wherein said immunoglobin Fc region is a human immunoglobin Fc region.

61. (New) A composition comprising the polypeptide of claim 53, and a carrier.

62. (New) An isolated polypeptide comprising amino acids 1 to 360 of SEQ ID NO:2.

63. (New) The polypeptide of claim 62, comprising amino acids -50 to 360 of SEQ ID NO:2.

64. (New) The polypeptide of claim 63, comprising amino acids -51 to 360 of SEQ ID NO:2.

65. (New) The polypeptide of claim 62, which binds TRAIL.

66. (New) The polypeptide of claim 62, which induces apoptosis.

67. (New) The polypeptide of claim 62, which is produced by a recombinant host cell.

68. (New) The polypeptide of claim 67, wherein said recombinant host cell is a eukaryotic host cell.

69. (New) The polypeptide of claim 62, which comprises a heterologous polypeptide.

70. (New) The polypeptide of claim 69, wherein said heterologous polypeptide comprises an immunoglobin Fc region.

71. (New) The polypeptide of claim 70, wherein said immunoglobin Fc region is a human immunoglobin Fc region.

72. (New) A composition comprising the polypeptide of claim 62, and a carrier.

73. (New) An isolated polypeptide comprising an amino acid sequence at least 90% identical to amino acids 134 to 157 of SEQ ID NO:2, wherein a DR5 variant consisting of amino acids 1 to 360 of SEQ ID NO:2, with the exception that amino acids 134 to 157 of SEQ ID NO:2 are deleted and replaced with said amino acid sequence, is anchored into the cell membrane and induces apoptosis.

74. (New) The polypeptide of claim 73, comprising acid sequence at least 95% identical to amino acids 134 to 157 of SEQ ID NO:2.

75. (New) The polypeptide of claim 74, which comprises amino acids 134 to 157 of SEQ ID NO:2.

76. (New) The polypeptide of claim 73, which is produced by a recombinant host cell.

77. (New) The polypeptide of claim 76, wherein said recombinant host cell is a eukaryotic host cell.

78. (New) The polypeptide of claim 73, which comprises a heterologous polypeptide.

79. (New) The polypeptide of claim 78, wherein said heterologous polypeptide comprises an immunoglobin Fc region.

80. (New) The polypeptide of claim 79, wherein said immunoglobin Fc region is a human immunoglobin Fc region.

81. (New) An isolated polypeptide comprising an amino acid sequence at least 90% identical to amino acids 158 to 360 of SEQ ID NO:2, wherein a DR5 variant consisting of amino acids 1 to 360 of SEQ ID NO:2, with the exception that amino

acids 158 to 360 of SEQ ID NO:2 are deleted and replaced with said amino acid sequence induces apoptosis.

82. (New) The polypeptide of claim 81, comprising an amino acid sequence at least 95% identical to amino acids 158 to 360 of SEQ ID NO:2.

83. (New) The polypeptide of claim 82, which comprises amino acids 158 to 360 of SEQ ID NO:2.

84. (New) The polypeptide of claim 81, which is produced by a recombinant host cell.

85. (New) The polypeptide of claim 84, wherein said recombinant host cell is a eukaryotic host cell.

86. (New) The polypeptide of claim 81, which comprises a heterologous polypeptide.

87. (New) The polypeptide of claim 86, wherein said heterologous polypeptide comprises an immunoglobin Fc region.

88. (New) The polypeptide of claim 87, wherein said immunoglobin Fc region is a human immunoglobin Fc region.

89. (New) A composition comprising the polypeptide of claim 81, and a carrier.

90. (New) An isolated polypeptide comprising an amino acid sequence at least 90% identical to amino acids 273 to 340 of SEQ ID NO:2, wherein a DR5 variant consisting of amino acids 1 to 360 of SEQ ID NO:2, with the exception that amino acids 273 to 340 of SEQ ID NO:2 are deleted and replaced with said amino acid sequence induces apoptosis.

91. (New) The polypeptide of claim 90, comprising an amino acid sequence at least 95% identical to amino acids 273 to 340 of SEQ ID NO:2.

92. (New) The polypeptide of claim 91, which comprises amino acids 273 to 340 of SEQ ID NO:2.

93. (New) The polypeptide of claim 90, which is produced by a recombinant host cell.

94. (New) The polypeptide of claim 93, wherein said recombinant host cell is a eukaryotic host cell.

95. (New) The polypeptide of claim 90, which comprises a heterologous polypeptide.

96. (New) The polypeptide of claim 95, wherein said heterologous polypeptide comprises an immunoglobin Fc region.

97. (New) The polypeptide of claim 96, wherein said immunoglobin Fc region is a human immunoglobin Fc region.

98. (New) A composition comprising the polypeptide of claim 90, and a carrier.

99. (New) An isolated polypeptide comprising an amino acid sequence at least 90% identical to the mature amino acid sequence encoded by the cDNA clone in ATCC Deposit No. 97920, wherein said polypeptide binds TRAIL.

100. (New) The polypeptide of claim 99, which induces apoptosis.

101. (New) The polypeptide of claim 99, comprising an amino acid sequence at least 95% identical to the mature amino acid sequence encoded by the cDNA clone in ATCC Deposit No. 97920.

102. (New) The polypeptide of claim 99, which is produced by a recombinant host cell.

103. (New) The polypeptide of claim 102, wherein said recombinant host cell is a eukaryotic host cell.

104. (New) The polypeptide of claim 99, which comprises a heterologous polypeptide.

105. (New) The polypeptide of claim 104, wherein said heterologous polypeptide comprises an immunoglobin Fc region.

106. (New) The polypeptide of claim 105, wherein said immunoglobin Fc region is a human immunoglobin Fc region.

107. (New) A composition comprising the polypeptide of claim 99, and a carrier.

108. (New) An isolated polypeptide comprising an amino acid sequence at least 90% identical to the full length amino acid sequence encoded by the cDNA clone in ATCC Deposit No. 97920, wherein said polypeptide binds TRAIL.

109. (New) The polypeptide of claim 108, which induces apoptosis.

110. (New) The polypeptide of claim 108, comprising an amino acid sequence at least 95% identical to the full length amino acid sequence encoded by the cDNA clone in ATCC Deposit No. 97920.

111. (New) The polypeptide of claim 108, which is produced by a recombinant host cell.

112. (New) The polypeptide of claim 111, wherein said recombinant host cell is a eukaryotic host cell.

113. (New) The polypeptide of claim 108, which comprises a heterologous polypeptide.

114. (New) The polypeptide of claim 113, wherein said heterologous polypeptide comprises an immunoglobin Fc region.

115. (New) The polypeptide of claim 114, wherein said immunoglobin Fc region is a human immunoglobin Fc region.

116. (New) A composition comprising the polypeptide of claim 108, and a carrier.

117. (New) An isolated polypeptide comprising the mature amino acid sequence encoded by the cDNA clone in ATCC Deposit No. 97920.

118. (New) The isolated polypeptide of claim 117, comprising the full length amino acid sequence encoded by the cDNA clone in ATCC Deposit No. 97920.

119. (New) The polypeptide of claim 117, which binds TRAIL.

120. (New) The polypeptide of claim 117, which induces apoptosis.

121. (New) The polypeptide of claim 117, which is produced by a recombinant host cell.

122. (New) The polypeptide of claim 121, wherein said recombinant host cell is a eukaryotic host cell.

123. (New) The polypeptide of claim 117, which comprises a heterologous polypeptide.

124. (New) The polypeptide of claim 123, wherein said heterologous polypeptide comprises an immunoglobin Fc region.

125. (New) The polypeptide of claim 124, wherein said immunoglobin Fc region is a human immunoglobin Fc region.

126. (New) A composition comprising the polypeptide of claim 117, and a carrier.

127. (New) An isolated polypeptide comprising at least 50 contiguous amino acids of amino acids 1 to 360 of SEQ ID NO:2, wherein said at least 50 contiguous amino acids binds an antibody with specificity for the polypeptide consisting of amino acids 1 to 360 of SEQ ID NO:2.

128. (New) The polypeptide of claim 127, which is produced by a recombinant host cell.

129. (New) The polypeptide of claim 128, wherein said recombinant host cell is a eukaryotic host cell.

130. (New) The polypeptide of claim 127, which comprises a heterologous polypeptide.

131. (New) The polypeptide of claim 130, wherein said heterologous polypeptide comprises an immunoglobin Fc region.

132. (New) The polypeptide of claim 131, wherein said immunoglobin Fc region is a human immunoglobin Fc region.

133. (New) A composition comprising the polypeptide of claim 127, and a carrier.

134. (New) An isolated polypeptide comprising an amino acid sequence at least 90% identical to 30 contiguous amino acids of amino acids 158 to 360 of SEQ ID NO:2, wherein said at least 30 contiguous amino acids binds an antibody with specificity for the polypeptide consisting of amino acids 1 to 360 of SEQ ID NO:2.

135. (New) The polypeptide of claim 134, comprising an amino acid sequence at least 95% identical to 30 contiguous amino acids of amino acids 158 to 360 of SEQ ID NO:2.

136. (New) The polypeptide of claim 135, comprising 30 contiguous amino acids of amino acids 158 to 360 of SEQ ID NO:2.

137. (New) The polypeptide of claim 134, which is produced by a recombinant host cell.

138. (New) The polypeptide of claim 137, wherein said recombinant host cell is a eukaryotic host cell.

139. (New) The polypeptide of claim 134, which comprises a heterologous polypeptide.

140. (New) The polypeptide of claim 139, wherein said heterologous polypeptide comprises an immunoglobin Fc region.

141. (New) The polypeptide of claim 140, wherein said immunoglobin Fc region is a human immunoglobin Fc region.

142. (New) A composition comprising the polypeptide of claim 134, and a carrier.

143. (New) An isolated polypeptide comprising an amino acid sequence at least 90% identical to 50 contiguous amino acids of amino acids 158 to 360 of SEQ ID NO:2.

144. (New) The polypeptide of claim 143, comprising an amino acid sequence at least 95% identical to 50 contiguous amino acids of amino acids 158 to 360 of SEQ ID NO:2.

145. (New) The polypeptide of claim 144, comprising 50 contiguous amino acids of amino acids 158 to 360 of SEQ ID NO:2.

146. (New) The polypeptide of claim 143, which is produced by a recombinant host cell.

147. (New) The polypeptide of claim 146, wherein said recombinant host cell is a eukaryotic host cell.

148. (New) The polypeptide of claim 143, which comprises a heterologous polypeptide.

149. (New) The polypeptide of claim 148, wherein said heterologous polypeptide comprises an immunoglobin Fc region.

150. (New) The polypeptide of claim 149, wherein said immunoglobin Fc region is a human immunoglobin Fc region.

151. (New) A composition comprising the polypeptide of claim 143, and a carrier.

152. (New) An isolated polypeptide comprising an amino acid sequence at least 90% identical to amino acids 1 to 133 of SEQ ID NO:2, wherein said polypeptide binds TRAIL.

153. (New) The polypeptide of claim 152, comprising an amino acid sequence at least 95% identical to amino acids 1 to 133 of SEQ ID NO:2.

154. (New) The polypeptide of claim 152, which is produced by a recombinant host cell.

155. (New) The polypeptide of claim 154, wherein said recombinant host cell is a eukaryotic host cell.

156. (New) The polypeptide of claim 152, which comprises a heterologous polypeptide.

157. (New) The polypeptide of claim 156, wherein said heterologous polypeptide comprises an immunoglobin Fc region.

158. (New) The polypeptide of claim 157, wherein said immunoglobin Fc region is a human immunoglobin Fc region.

159. (New) A composition comprising the polypeptide of claim 152, and a carrier.

160. (New) An isolated polypeptide comprising amino acids 1 to 133 of SEQ ID NO:2.

161. (New) The polypeptide of claim 160, which binds TRAIL.

162. (New) The polypeptide of claim 160, which is produced by a recombinant host cell.

163. (New) The polypeptide of claim 162, wherein said recombinant host cell is a eukaryotic host cell.

164. (New) The polypeptide of claim 160, which comprises a heterologous polypeptide.

165. (New) The polypeptide of claim 164, wherein said heterologous polypeptide comprises an immunoglobin Fc region.

166. (New) The polypeptide of claim 165, wherein said immunoglobin Fc region is a human immunoglobin Fc region.

167. (New) A composition comprising the polypeptide of claim 160, and a carrier.

168. (New) An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) amino acids 11 to 59 of SEQ ID NO:2;

(b) amino acids 68 to 103 of SEQ ID NO:2;

(c) amino acids 173 to 220 of SEQ ID NO:2; and

(d) amino acids 224 to 319 of SEQ ID NO:2;

wherein said polypeptide binds an antibody with specificity for the polypeptide of amino acids 1 to 360 of SEQ ID NO:2.

169. (New) The polypeptide of claim 168 comprising amino acids 11 to 59 of SEQ ID NO:2.

170. (New) The polypeptide of claim 168 comprising amino acids 68 to 103 of SEQ ID NO:2.

171. (New) The polypeptide of claim 168 comprising amino acids 173 to 220 of SEQ ID NO:2.

172. (New) The polypeptide of claim 168 comprising amino acids 224 to 319 of SEQ ID NO:2.

173. (New) The polypeptide of claim 168, which is produced by a recombinant host cell.

174. (New) The polypeptide of claim 173, wherein said recombinant host cell is a eukaryotic host cell.

175. (New) The polypeptide of claim 168, which comprises a heterologous polypeptide.

176. (New) The polypeptide of claim 175, wherein said heterologous polypeptide comprises an immunoglobin Fc region.

177. (New) The polypeptide of claim 176, wherein said immunoglobin Fc region is a human immunoglobin Fc region.

178. (New) A composition comprising the polypeptide of claim 168, and a carrier.

179. (New) A composition comprising the polypeptide of claim 73, and a carrier.

Remarks

The specification has been amended to correct informalities and typographical errors. The claims have been amended to more particularly point out and distinctly claim the subject matter Applicants regard as the invention.

Support for the amendments to the specification is found throughout the specification as filed. More particularly, the specification has been amended to reposition and update the claim of priority benefit, to reflect the new address of the American Type Culture Collection, to comply with 37 C.F.R. § 1.821(b), and to correct typographical errors.

Reference to sequence identifiers has been added to the brief description of Figure 4. In addition, typographical errors have been corrected. With respect to the correction on page 9, line 36, it is clear from a comparison of Figure 1 and SEQ ID NO:2 that amino acids 1 to 51 in Figure 1 correspond to amino acids -51 to -1 in SEQ ID NO:2.

With respect to the correction of the NaCl and sodium citrate concentrations on page 12, lines 24-25 of the specification, Applicants submit that 5x SSC is a well-known solution used in hybridization solutions. SSC is normally made as a 20x stock solution, and then diluted accordingly for a particular use. The 20x SSC stock solution contains 3 M NaCl and 0.3 M trisodium citrate. *See, e.g., Gibco BRL Products and Reference Guide, 2000-2001* at page 22-24 (Exhibit A). To make a 5x SSC solution, the 20x solution must be diluted by one-fourth. Therefore, a 5x SSC solution contains 750 mM NaCl (3 M ÷ 4 = 750 mM) and 75 mM trisodium citrate (0.3 M ÷ 4 = 75 mM). One skilled in the art would have immediately recognized that the amount of ingredients listed in the specification for a 5x SSC solution was incorrect. Rather than describing a 5x SSC solution, made

up of 750 mM NaCl and 75 mM trisodium citrate, the specification inaccurately listed the ingredient amounts for a 1x solution. The skilled artisan, in recognizing the typographical error, could have easily adjusted the amount of ingredients described in the specification to properly make a 5x SSC solution.

On page 12, line 26, Applicants have noted a typographical error in the amount of salmon sperm DNA. The inclusion of agents such as salmon sperm DNA as blocking agents is well known in the art. *See, e.g.,* Ausubel, *et al.*, *Current Protocols in Molecular Biology*, John Wiley & Sons, Inc., (1997) at page 2.10.7 (Exhibit B). One skilled in the art would know that salmon sperm DNA is present in hybridization solutions in μg/ml quantities and thus would immediately recognize the above-described typographical error in the specification. *See id.* Further, the skilled artisan, in recognizing the typographical error, could easily have adjusted the amount of ingredients described in the specification to properly included 20 μg/ml denatured, sheared salmon sperm DNA in the hybridization solution.

Therefore, because no new matter will be added to the specification if these typographical errors are corrected, Applicants respectfully request that the amendments to the specification be entered.

Claims 1-34 have been canceled without prejudice to or disclaimer of the subject matter therein. Claims 35-179 have been added. Support for the claims can be found throughout the specification and the original claims. Specifically, support for claims 44-46, 53-55, 62-66, 73-75, 81-83, 90-92, 99-101, 108-110, 117-120, 127, 134-136, 143-145, 152-153, 160-161, and 168-172 can be found, for example, in the specification at page 6, lines 20-28, page 26, lines 14-27, page 28,

line 27 to page 29, line 4, page 29, line 28 to page 30, line 8 and Examples 5 and 6. Support for claims 38-39, 47-48, 56-57, 67-68, 76-77, 84-85, 93-94, 102-103, 111-112, 121-122, 128-129, 137-138, 146-147, 154-155, 162-163, 173-174 can be found, for example, in the specification at page 21, lines 22-29. Support for claims 40-42, 49-51, 58-60, 69-71, 78-80, 86-88, 95-97, 104-106, 113-115, 123-125, 130-132, 139-141, 148-150, 156-158, 164-166, and 175-177 can be found, for example, in the specification at page 22, lines 3-6 and page 53, lines 30-31. Support for claims 45, 56, 65, 74, 83, 93, 103, 110, 121, 129, 137 and 148 can be found, for example, in the specification at page 40, lines 17-36. The new claims add no new matter and their entry is respectfully requested.

Inventorship

The inventors of the subject matter of the present application are Jian Ni, Reiner L. Gentz, Guo-Liang Yu, and Craig Rosen. Applicants have discovered that due to an inadvertent error Jeffery Su was originally named as an inventor in the parent application, U.S. Application Serial No. 09/042,583, but should not have been so named. Applicants note that under 37 C.F.R. § 1.53(b)(1) and 37 C.F.R. § 1.63(d)(1)(ii), a newly executed oath or declaration is not necessary when inventors are only being deleted. Accordingly, under 37 C.F.R. § 1.63(d)(2), Applicants respectfully request Jeffery Su be removed as an inventor.

Conclusion

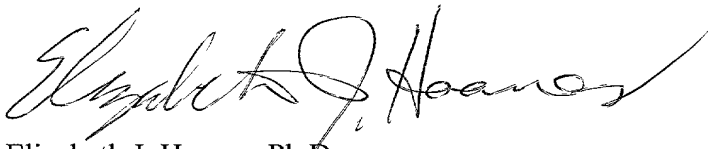
It is respectfully believed that this application is now in condition for substantive examination. Early notice to this effect is respectfully requested.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



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Version with markings to show changes made

Inventorship:

Jeffrey Su has been deleted as an inventor.

In the Specification:

The following priority information has been inserted below the heading "Field of the Invention" on page 1:

This present application is a divisional of U.S. Appl. No. 09/042,583, filed March 17, 1998, which claims the benefit of U.S. Provisional Appl. Nos. 60/040,846, filed March 17, 1997 and 60/054,021, filed July 29, 1997, all of said applications are herein incorporated by reference.

The entire paragraph at page 1, lines 12-14 has been deleted.

The paragraph beginning at page 6, line 30 with the following paragraph:

FIG.4 shows the nucleotide sequences (HAPBU13R (SEQ ID NO:6) and HSBBU76R (SEQ ID NO:7)) of two cDNA molecules which are related to the nucleotide sequence shown in Figure 1 (SEQ ID NO:1).

The paragraph beginning at page 7, line 20, with the following paragraph:

The present invention provides isolated nucleic acid molecules comprising a polynucleotide encoding a DR5 polypeptide having the amino acid sequence shown in FIG. 1 (SEQ ID NO:2), or

a fragment of the polypeptide. The DR5 polypeptide of the present invention shares sequence homology with other known death domain containing receptors of the TNFR family including human TNFR- I, DR3 and Fas (FIG. 2). The nucleotide sequence shown in FIG. 1 (SEQ ID NO:l) was obtained by sequencing cDNA clones such as HLYBX88, which was deposited on March 7, 1997 at the American Type Culture Collection, [12301 Park Lawn Drive, Rockville, Maryland 20852]10801 University Boulevard, Manassas, Virginia 20110-2209, and given Accession Number 97920. The deposited clone is contained in the pSport 1 plasmid (Life Technologies, Gaithersburg, MD).

The paragraph beginning at page 9, line 25, with the following paragraph:

In the present case, the predicted amino acid sequence of the complete DR5 polypeptide of the present invention was analyzed by a computer program ("PSORT"). See, K. Nakai and M. Kanehisa, Genomics 14:897-911 (1992). PSORT is an expert system for predicting the cellular location of a protein based on the amino acid sequence. As part of this computational prediction of localization, the methods of McGeoch and von Heinje are incorporated. The analysis by the PSORT program predicted the cleavage sites between amino acids 51 and 52 in Figure 1 (-1 and 1 in SEQ ID NO:2). Thereafter, the complete amino acid sequences were further analyzed by visual inspection, applying a simple form of the (-1,-3) rule of von Heinje. von Heinje, supra. Thus, the leader sequence for the DR5 protein is predicted to consist of amino acid residues from about 1 to about 51, underlined in Figure 1 (corresponding to about -51 to about [1]-1 in SEQ ID NO:2), while the predicted mature DR5 protein consists of residues from about 52 to about 411 in Figure 1 (corresponding to about 1 to about 360 in SEQ ID NO:2).

The paragraph beginning at page 12, line 19, with the following paragraph:

In another aspect, the invention provides an isolated nucleic acid molecule comprising a polynucleotide which hybridizes under stringent hybridization conditions to a portion of the polynucleotide in a nucleic acid molecule of the invention described above, for instance, the cDNA clones contained in ATCC Deposit No. 97920. By "stringent hybridization conditions" is intended overnight incubation at 42°C in a solution comprising: 50% formamide, 5x SSC ([150]750 mM NaCl, [15mM]75 mM tri sodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 [g/ml]µg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1x SSC at about 65°C.

In the Claims:

Claims 1-34 are canceled.

Claims 35-179 have been newly added.